IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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| Application of: | Docket No.: 31927-CIP2 |
| MESSADEK, Jallal | Confirmation No.: 6961 |
| Serial No.: 10/635,048 | Group Art Unit No.: 1617 |
| Filed: August 4, 2003 | Customer No.: 23589 |
| GLYCINE BETAINE AND ITS USE | Examiner: Betton, Timothy E. |

Commissioner for Patents
Mail Stop Amendment
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

DECLARATION UNDER 37 C.F.R. § 1.132

I, Jallal Messadek, do declare and state as follows:

1. I am a citizen of Belgium and reside in Liège, Belgium. I am over the age of eighteen, under no disability, fluent in English, and understand the following statements made regarding the above-referenced patent application and the prior art references cited by the Examiner. I am also the inventor named in the above referenced patent application.

2. I understand that the Examiner has rejected the claims as being obvious in view of Ushiyama et al. (USPN 4,605,548), D'Angelo et al. (USPN 5,405,614), Mitragotri et al. (USPN 5,814,599), Cleary (USPN 4,911,916), and Malamud et al. (USPN 5,928,195). I have reviewed the Examiner's rejections and the cited references. I have been asked to provide this declaration to explain what these references would have taught to one of ordinary skill in the art at the time of filing the present application and to attest to the nonobviousness of the invention.

3. On page 8 of the Office Action, the Examiner asserts:

"All references above do not teach glycine betaine. However, Malamud et al. teach compounds containing a betaine compound (note the term *betaine* is interchangeable with the term glycine betaine) (co1.5, 1. 38)."

In view of this statement, I note two things:

a. Examiner recognizes that **none** of the cited Ushiyama et al. (USPN 4,605,548), D'Angelo et al. (USPN 5,405,614), Mitragotri et al. (USPN 5,814,599), and Cleary (USPN 4,911,916) teach glycine betaine.

b. According to Examiner, such deficiencies should be resolved by the Malamud reference, and particularly col. 5, line 38 where Malamud is thought to teach or to suggest the compound claimed.

However, even if the term "betaine" could be considered interchangeable with the term "glycine betaine," (although Applicant is not conceding this point), **neither** "betaine," nor "glycine betaine" can be interchangeable with the "alkyl-*N*-betaine surfactants" disclosed in Malamud. More specifically, the term "betaine" occurs twice in the Malamud reference (col. 5, line 38 and claim 8), and it is **never** written simply as "betaine" alone, but as an "alkyl-*N*-betaine surfactant." This is not the same compound as "betaine" or "glycine betaine."

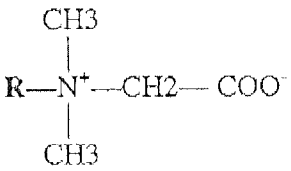
4. The alkyl-*N*-betaine surfactants are disclosed and claimed by Malamud with reference to 3 U.S. patents, which precisely describe such compounds. In effect, one can read in Malamud reference, column 5, lines 34-43 (which encompass line 38 cited by the Examiner):

> "For an intravaginal microbicide device, the preferred drug may comprise a surfactant with spermicidal, antiviral, antibacterial, and antifungal activities, such as a class of compounds comprising as a first component an alkyl-N-betaine surfactant and as a second compound an oxide selected from the group consisting of alkyl-N, N-dimethyl amine oxide, N-dihydroxyethylamine oxide, acylamino t-amine oxide and mixtures thereof, as disclosed in U.S. Pat. Nos. 4,107,328, 4,839,158 and 5,314,917, the disclosures of which are hereby incorporated herein by reference."

In effect, these 3 patents, namely U.S. Patent Nos. 4,107,328, 4,839,158, and 5,314,917, describe beyond any doubt by structural drawings what are the claimed "alkyl-*N*-betaine surfactants" taught by the Malamud reference. It is noted that structural drawings are used in chemistry by those skilled in the art to clearly establish and without controversy the identity of a given molecule. For ease of reference, the alkyl-*N*-betaine structures disclosed in the patents referenced by Malamud have been reproduced below.

U.S. Patent No. 4,107,328 recites:

"In general, a first component, namely, alkyl-N-betaine surfactant employed as a non-ionizing zwitterion can be written as:

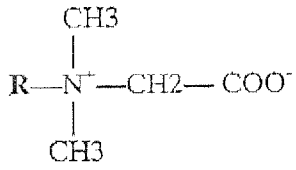


Where **R** is a higher alkyl having from **10 to 18 carbon atoms**. Illustrative of such alkyl-N-betaine is coco-N-betaine, cetyl-N-betaine, stearyl-N-betaine, isostearyl-35 N-betaine, or oleyl-N-betaine, or mixtures of the same." (col. 2 lines 23-36).

In the same manner, claim 1 of the '328 patent refers to the same general formula with **R** being a higher alkyl having from **10 to 18 carbon atoms.**

U.S. Patent No. 4,839,158 recites:

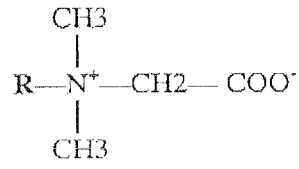
"... a higher alkyl-N-betaine having the structure"



"where **R** is a higher alkyl having from **10 to 18 carbon atoms**." (Abstract, col. 2, 14-49, and claim 1).

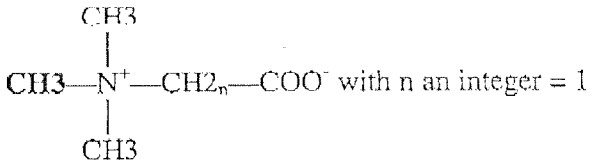
U.S. Patent No. 5,314,917 recites:

"...alkyl-N-betaines have structure as follows"



"where **R** is a higher alkyl group having from **10 to 18 carbon atoms, preferably from 12-16 carbon atoms**." (col. 4, line 48-col. 5, line 18).

In contrast, the claimed compound has the following structure:




That is, "**R**" is a $CH_3$ group having **1 carbon atom**.

Thus, the claimed compound simply cannot be considered to be equivalent to the "alkyl-*N*-betaine surfactants" disclosed in Malamud, because the shortest alkyl chain disclosed for the alkyl-*N*-betaine surfactants in Malamud has 10 carbon atoms. That is, those skilled in the art would immediately recognize that 1 carbon atom is not the same at 10-18 carbon atoms, and that the claimed compounds have different structures, with different functionalities, and are simply different compounds from the disclosed alkyl-*N*-betaine surfactants disclosed in Malamud.

5. Moreover, when R is a methyl group having 1 carbon atom, as in the claimed structure, it is impossible to also link a higher alkyl group having from 10 to 18 carbon atoms to the $-CH_3$ group or to the ammonium ($N^+$). That is, under basic chemistry principles, the four single bonds of the carbon in the methyl group are already bound to 3 hydrogen atoms and to the ammonium cation. Thus, the carbon of the $-CH_3$ group is saturated and cannot support any additional bonds. It is simply impossible to have in addition a higher alkyl group having from 10 to 18 carbon atoms bound to the $-CH_3$ group or to the ammonium cation. Hence, according to basic laws of chemistry the two structures (glycine betaine and alkyl-*N*-betaine surfactant) cannot coexist in the same molecule. Therefore, Malamud et al. teach compounds **that cannot contain** the compound as claimed simply because if $CH_3$ is present as the **R** group and linked to $N^+$, it is impossible to bind a higher alkyl group having from 10 to 18 carbon atoms to this structure.

6. In order to arrive at the claimed invention, one of ordinary skill in the art would have had to:

a. Ignore the state of the art regarding the use of alkyl-*N*-betaine surfactants according to the above formulas where R is a higher alkyl having from 10 to 18 carbon atoms;
b. Ignore that such alkyl long chains are responsible for the microbicide effects of the surfactant, as stated by Malamud himself, and clearly established by the published art (Exhibit B, page 2515, Discussion 2nd paragraph);
c. Select a compound below the cutoff for microbicidal efficacy as defined by Malamud;
d. Replace the higher alkyl chain having from 10 to 18 carbon atoms with a methyl group having only 1 carbon atom; and
e. Ignore that the compound resulting therefrom (glycine betaine) is known to *favor* bacterial and microbial growth, i.e. having **opposite** properties of those sought in Malamud.

It is respectfully submitted that one of ordinary skill in the art would not have been motivated to make all of these modifications to the disclosure of Malamud, contrary to accepted knowledge, *and then* combine this with four other references to arrive at the claimed invention. Accordingly, the present invention would not have been obvious to one of ordinary skill in the art at the time of the present invention based upon the teachings of the cited references.

7. I further declare that all statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that wilful, false statements and the like are punishable by fine or imprisonment, or both, under § 1001 of Title 18 of the United States Code, and such wilful false statements may jeopardize the validity of any patents issued from the patent application.

Date: Vège October 15th, 2008

Jalal Messadek
Applicant & Inventor